REMARKS

Claims 1-10 were rejected in an Office Action mailed May 18, 2006 ("Office Action"). Please reconsider the rejections in view of the foregoing amendments and remarks as set forth herein. Instant claims 36-43 correspond to claims 1-10, which were subject to examination and the rejections set forth in the Office Action.

I. Rejection under 35 USC §112, second paragraph

The rejection of claims 36-43 (canceled claims 1-10) is respectfully traversed for reasons set forth herein. The Examiner asserts that the inventions are not particularly pointed out or distinctly claimed for a plurality of response, each of which is addressed herein below.

1. **Claim 36 (canceled claims 1 and 7)**

Regarding claim 36, the claim particularly points out and distinctly claims a system comprising at least two components. In particular, claim 36 plainly recites an "Integrated biosensor and simulation system comprising: a sensor...and a simulator...". Therefore, the claim is clear and definite, because it would be understood that the claim is directed to an integrated system comprising a biosensor and simulation component. Furthermore, canceled claims 36-46 (claims 1-10) were previously understood to be system claims, where the Examiner asserted that claims 1-10 are directed to "a system and method" and claims 11-20 are directed to a network biosensor. (See, Restriction, mailed Feb. 28, 2006).

In any event, the claims must not be examined in a vacuum, but rather, must be interpreted in view of the full disclosure. Thus, in reading the specification (e.g., "Summary" section), one would comprehend that an "Integrated biosensor-simulation system combines one or more sensor to detect various conditions...and...simulator...". Therefore, the claim 1 is clear and definite as written.

Next, the Examiner asserts that it is unclear whether claim 36 is directed to a simulator that generates an output or whether a simulator uses a signal and a model wherein the model generates an output (i.e., therapeutic or diagnostic). Again, the plain meaning of the subject phrase is clear and definite, where claim 36 recites "a simulator for using the signal *and* a model of the target to generate a therapeutic or diagnostic output." (emphasis added) Clearly, the conjunction "and"

should indicate to the reader that the simulator utilizes the signal generated from the sensor, *and* a model for the biological target to generate an output (i.e., therapeutic or diagnostic). Furthermore, the specification provides ample characterization of a "simulator using system-biology model *and* sensor data adaptively to provide therapy, diagnosis, or other automated feedback [i.e., output]." (e.g., Summary section). Therefore, claim 1 is clear and definite as written.

2. Claim 36 (canceled claim 2)

Regarding claim 37, the Examiner asserts that it is unclear whether the claim is directed to an intended use of the sensor and/or the simulator and/or a result. Further, the Examiner asserts that it is unclear "what limitation of the sensor and simulator is intended". With respect to this latter assertion, it is not understood what is the source of the Examiner's misapprehension. The plain meaning of the limitation "the sensor is reconfigurable by the simulator" is unambiguous and distinct. The specification is replete with characterizations for sensor(s) that are reconfigurable (e.g., paragraphs[1] 0004, 0021-22, 0218, 0224, 0232). As the instant specification clearly sets forth, in one embodiment, a *reconfigurable* biocatalytic chip are software programmable from the simulator (e.g., systems-biology platform or through wireless external communication unit), which can result in activation, deactivation, manufactured or disassembled). (e.g., paragraph 0224). In another embodiment, "reconfigurable" means a sensor(s) can be personalized by the simulator, so that the sensor (e.g., tissue scaffold) is reconfigured based on the individual need. (e.g., paragraph 0225).

Therefore, whether reading the claim or the specification, it is quite unambiguous that the sensor(s) is reconfigurable by the simulator.

The Examiner's reference to an intended use or a result appears to be an extension of the misapprehension as to what is being claimed. Claim 36 merely recites that the sensor is reconfigurable by the simulator. Thus, it is not a result that is being reconfigured but the sensor. Further, the limitation is more than a mere intended use, because claim 36 is directed to a system where a sensor is capable of being reconfigured by a simulator and a simulator is capable of

[1] All references to the application/specification correspond to the published application, i.e., No. 2005/0043894A1)

reconfiguring the sensor. In other words, the subject limitation characterizes a material aspect of the system, with respect to the simulator and sensor. Therefore, claim 2 is clear and definite as written.

3. Claim 37 (canceled claim 3)

Regarding claim 37, the Examiner asserts that it is unclear what further limitation is intended with respect to the base claim 36. Claim 37 further limits the number/type of signal detected. For example, where base claim 36 is directed to a sensor for sensing a biological signal, dependent claim 38 further limits the base claim because the sensor is capable of sensing a second signal from a food material. The claim recites that the sensor generates a second signal which generates an output. The claim is directed to a system, so it is unclear why the Examiner refers to "method steps". (Office Action, page 9, lines 12-15).

Further, the plain meaning of claim 37 is unambiguous, where a signal corresponds to a biological target, as required by independent claim 36, and a *second* signal corresponds to a food material for consumption by the biological target. Therefore, one should comprehend claim 38 to further require a second signal, different from the first signal. In addition, the food material is not required to *have been* consumed. As written the claim, as further characterized in the specification, requires that the food material is sensed to produce a second signal, but there is no requirement that the sensor sense the food material after consumption (See, paragraphs 0106, 0154, 0157 and 0187-0189).

Regarding whether the simulator utilizes only the second signal or the first signal to produce an output, it is respectfully pointed out that since claim 38 (canceled claim 3) is a dependent claim, it incorporates the intervening claimed limitations. Therefore, as written, the claim requires both the first and second signal to produce an output.

Similarly, regarding whether the model of the base claim is also used in conjunction with the signals, claim 37is a dependent claim, thus one would readily comprehend that all the limitations of intervening claims are required (e.g., signal in base claim, model in base claim and second signal in instant dependent claim 38).

4. Claim 38 (canceled claim 4)

Regarding claim 38 the Examiner asserts that it is unclear what is "a regulatory condition" . The Examiner actually sets forth several different examples for interpretations of the term "regulatory condition", all of which fall within the scope of the limitation. Therefore, this is not a case of indefiniteness, but breadth or scope of the subject limitation. It is respectfully pointed out that the breadth of claims is not to be equated with indefiniteness. MPEP § 2173.04.

Furthermore, as to the issue raised with the limitation "the output", it is clear that the instant claim has antecedent support for the output as being "a therapeutic *or* diagnostic output". Therefore, it is not indefinite as to what is the output, since the plain meaning of output encompasses therapeutic or diagnostic.

5. Claim 39 (canceled claim 5)

The Examiner asserts that the limitation "couples" is vague, because it is not known whether this requires a physical connection or connection via a network. Further, the Examiner asserts that it is unclear whether "coupling" is a method step.

The claim requires that a sensor "couples to the simulator via a programmable switch". As recited in the base claim and further characterized in the specification, the components of the system can be physically coupled or coupled through communications such as wireless communications. (e.g., paragraphs 0005, 0019, 0021, 0049). Therefore, it appears there is a misapprehension of scope versus any issues of indefiniteness.

6. Claim 40 (canceled claims 6 and 7)

The Examiner asserts that it is unclear whether independent claim 41 is directed to a method or system. As the Examiner points out the claim is interpreted to mean it is directed to a method, thus it is unclear why this claim is rejected. The claim follows standard practice for reciting a method. Furthermore, all applicable dependent claims recite "The method...", obviating any purported ambiguity.

Regarding whether a signal and a model are utilized to generate an output, similar to the discussion above for the system claims, the method claim here is directed to simulating using the signal *and* model to generate an output. Again, the simulator generates the output using both the

signal and the model. The claim's plain meaning is distinct and clear. Furthermore, the specification is replete with description characterizing (e.g., paragraph 0098; describing a simulator compared sensed signals against a model or other software prediction to provide an output). In addition, the method requires generating an output. In sum, the plain meaning of the claim aloneor in conjunction with the specification is clear and distinct.

7. Claim 40 (canceled claim 7)

The Examiner asserts that is unclear whether "reconfiguring" is intended to be an additional step to "sensing" and "stimulating" recited in the base claim or is somehow to substitute one or more steps of the base claim. The claim is a dependent claim which further requires a simulator reconfigures a sensor. The plain meaning of the claim is clear and distinct, where an additional step of reconfiguration is required. Furthermore, the disclosure adequately characterizes the "reconfiguring" embodiment (e.g., paragraphs 0005, 0022, 0028, 0046, 0244).

8. Claim 41 (canceled claim 8)

The Examiner asserts the same grounds of rejection as those stated for claim 37. Claim 41(canceled claim 8) further limits the number/type of signal detected. For example, where the base claim is directed to a method requiring sensing, simulating and generating an output. Dependent claim 41 further limits the base claim because the sensor is capable of sensing a second signal from a food material.

Further, the plain meaning of claim 41 is unambiguous, where a signal corresponds to a biological target, as required by independent claim 40, and a *second* signal corresponds to a food material for consumption by the biological target. Therefore, one should comprehend claim 41to further require a second signal, different from the first signal. In addition, the food material is not required to *have been* consumed. As written the claim, as further characterized in the specification, requires that the food material is sensed to produce a second signal, but there is no requirement that the sensor sense the food material after consumption (See, paragraphs 0106, 0154, 0157 and 0187-0189).

9. Claim 43 (canceled claim 9)

The limitation "the output" is clear and distinct, because base claim clearly recites that output can be "therapeutic or diagnostic". Therefore, the instant claim encompasses therapeutic or diagnostic output.

In sum, the instant claims are clear and definite. Therefore, this rejection should be withdrawn.

II. Rejection under 35 USC § 112, first paragraph

Claims 1-10 (now claims 36-43) were canceled as failing to comply with the enablement requirement. This rejection is respectfully traversed. The Examiner sets forth *Wands* factors analysis, which is addressed in turn herein below. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1. Breadth of claims

The Examiner asserts that the claims are broad and that the specification does not provide specific guidance as to how to generate an unspecified signal, using an unspecified sensor, which senses an unspecified target, nor how to generate a diagnostic or therapeutic output.

There appears to be some misapprehension as to what are various key aspects of the invention. For example, as set forth in Figures 1-6, the invention is not limited to any particular sensor, target, simulator or output. Rather, one of the key aspects of the invention is the integration of various components in systems and methods to monitor individual, to simulate data and/or analyzing systems-biology software to generate diagnostic or therapeutic guidance.

Moreover, the specification provides numerous examples of the types of sensors that can be utilized with the methods or systems of the invention. For example, Figure 2 provides various sensors that can be utilized. Furthermore, Figure 1 illustrates a system envisaged by Applicant, which can be utilized in one or more methods of the invention. The system comprises a sensor unit, a systems biology platform which provides simulation (e.g., systems biology platform). Furthermore, the specification provides ample examples of sensors that are known in the art, such as MEMs, NEMS or microfluidic sensors (e.g., paragraphs 0050, 0052). Particular sensors disclosed include DNA sensors (e.g., paragraphs 0052, 0054, 0059), RNA sensors (e.g., paragraphs

0060, 0061), peptide/protein sensors (e.g., paragraphs 0062-0065), lipid/fatty acid sensor (e.g., paragraphs 0076), virus sensor (e.g., paragraph 0078) or carbohydrate sensor (e.g., paragraphs 0082). Therefore, specific examples of sensors and target molecules are adequately disclosed in the specification. Furthermore, the types of signals for various sensors are known in the art, as well as disclosed in the specification. (e.g., paragraph 0019). Moreover, the artisan will recognize that any sensor/target known in the art can be utilized in the methods/systems of the invention.

2. Nature of the invention

As discussed herein above, the claims are directed to a system and method comprising sensor and simulation components.

3. Prior art/predictability

The Examiner sets forth several examples of prior art systems for diagnosis of different conditions using various specific signals. (Office Action, pages 4-7). A patent need not teach, and preferably omits, what is well known in the art. Therefore, the Examiner appears to acknowledge that there are various sensors in the prior art that are utilized for provide signals, which can be utilized to generate an output, such as in diagnosis. Indeed, "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

Notably, the Examiner does not set forth a single reasoned basis as to why there is unpredictability in integrating various sensors into systems or methods of the present invention. As such, the Examiner has not met the burden of providing evidence to support the assertion that there is unpredictability in practicing the claimed inventions, which can lead to undue experimentation.

4. The level of skill

The level of skill in the art is high. Therefore, the artisan can integrate what is known in the art with the novel disclosures of the instant specification to make and use the system and methods of the invention.

5. Working examples

The Examiner asserts that there are no working examples presented and that the specification does not teach how to make and use the invention, because no specific sensor, target or simulators are disclosed. Furthermore, the Examiner asserts that the specification does not teach how to diagnose a disease/condition or teach a system comprising an actual biosensor and simulator.

First, compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. See, MPEP § 2164.02. An example may be "working" or "prophetic." A working example is based on work actually performed. A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved. An applicant need not have actually reduced the invention to practice prior to filing. In *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987), as of Gould's filing date, no person had built a light amplifier or measured a population inversion in a gas discharge. The Court held that "The mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it." 822 F.2d at 1078, 3 USPQ2d at 1304 (quoting *In re Chilowsky*, 229 F.2d 457, 461, 108 USPQ 321, 325 (CCPA 1956)).

Second, the instant specification provides ample description of various sensors, targets and simulators (e.g., Section II(1), supra). Examples of sensors/targets include a metabolite sensor can measure serum homocysteine levels associated with increased risk of cervical cancer. (paragraph 0086). Further, a DNA sensor may detect common polymorphisms in one-carbon metabolic pathway, including mutations such as MTHFR, C677T, A1298C. (Id.). Additional examples, include a chemical sensor which senses levels of carcinogen, benzo(a)pyrene diol epoxide, a metabolic product found in tobacco smoke, known to cause 9p21 aberrations in peripheral blood lymphocytes in bladder cancer. (paragraph 0085). Yet another example, discloses a sensor can

monitor blood-flow to provide a signal that can be indicative of arterial pulse pressure, which signal can be plethysmography signal that can be produced by an implantable or non-implanted sensor (paragraph 0092). Furthermore, various methods known in the art are disclosed as a means for implanting sensors. (e.g., paragraphs 0094-0095). The foregoing are but a few examples provided in the instant specification, which provides a multitude of examples, each of which is adaptable to systems or methods of the present invention.

In addition, the specification provides various examples for a simulator component to be utilized with one or more sensors of the invention, i.e., a system comprising a sensor and simulator (e.g., paragraph 0028-0029, 0041-0048). Therefore, in view of the foregoing, it is factually inaccurate to assert that the specification does not disclose a system comprising a sensor and a simulator, or that the specification does not teach how to use systems/methods of the invention to generate an output, such as diagnosing a condition.

6. Amount of experimentation

The Examiner asserts that undue experimentation is necessary, because one of skill must randomly select a sensor, target, and must guess which signal and model to use for generating an unknown therapeutic or diagnostic output. There appears to be a misapprehension of what an artisan understands and would do in order to practice the claimed inventions.

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). As evidenced by the examples provided in the instant specification or by the art that Examiner notes (Office Action, pages 4-7), various sensors are known in the art.

The instant inventions are directed to systems/methods of integrated sensors and simulators, and where simulators can reconfigure sensors as needed. This is not the case of random selection or guesswork. Rather, the artisan would utilize one or more sensors known in the art in the systems and methods of the invention. For example, a clinician wanting to sense a target in someone susceptible to cancer (e.g., heavy smoker) would select diagnostic metrics known in the art (e.g., selection of cancer markers using DNA sensor disclosed in the instant specification and/or known

in the art). One novel aspect of the invention is integrating a sensor with a simulator (e.g., systems-biology platform) to interpret data to be analyzed and modeled to determine the diagnostic or therapeutic output.

In sum, the reasons set forth in the Office Action fail to establish a prima facie case for lack of enablement. Therefore, this rejection should be withdrawn.

III. Rejections under 35 USC §102

1. US 6,042,548 (Giuffre)

Claims 1-2, 4-7 and 9-10 were rejected (new claims 36-43) as being anticipated by US Patent 6,042,548 (Giuffre). This rejection is respectfully traversed.

The claims are directed to systems and methods requiring a sensor, a simulator and where the sensor is reconfigurable by the simulator. The Examiner asserts that Guiffre discloses a simulation using a signal and a model, where a sensor is reconfigured by a simulator (citing Fig. 3 and col. 6, lines 53-59). The reference does not disclose a sensor that is reconfigured by a simulator. In fact, as the Examiner points out, the reference discloses that data from a cardiovascular monitor is utilized to crate a simulated brain monitor means signal which it compares with an actual brain monitor means signal, and using a series of comparator means, constructs a hybrid signal with decreased artifact. (col. 6, ll. 55-59). In other words, the simulator does not actually reconfigure the sensor, but rather, constructs a hybrid signal from two sets of sensors. This does not meet the claimed requirement of "reconfiguring a sensor".

As recited in the instant claims, "reconfigurable" does not equate to utilizing different sensors to produce a hybrid signal, as asserted by the Examiner. For example, the instant specification discloses in one embodiment, a biocatalytic chip which is software programmable from the simulator (e.g., systems-biology platform or through wireless external communication unit), which can result in activation, deactivation, manufactured or disassembled). (e.g., paragraph 0224). In another embodiment, "reconfigurable" means a sensor(s) can be personalized by the simulator, so that the sensor (e.g., tissue scaffold) is reconfigured based on the individual need. (e.g., paragraph 0225). Thus, reconfigured in this sense encompasses reconfiguring a sensor or

multiple sensors, and not merging two sets of signals to reduce background/noise, as Giuffre discloses.

As such, the reference does not anticipate independent claims 36 and 40. Therefore, this rejection should be withdrawn.

2. US 6,542,858 (Grass)

Claims 1-2, 4-7 and 9-10 (new claims 36-43) were rejected as being anticipated by US Patent 6,542,858 (Grass). This rejection is respectfully traversed.

First, it is respectfully pointed out that the reference is not available under 35 USC 102(b), because it was published in April 1, 2003, while the instant application was filed in August 22, 2003. Presumably, the Examiner intended to assert this rejection under 35 USC 102(e).

The Examiner asserts that Grass discloses reconfiguring a sensor by a simulator (citing col. 12, line 52 through col. 13, line 32). Again, there appears to be some misapprehension as to what is claimed and what is disclosed with respect to the limitation "reconfigures". Upon examination of the entirety of the Grass disclosure, as well as a closer examination of the portions that the Examiner cites, Grass states that values for a given simulation model can be generated de novo or obtained from existing sources and that optimized adjustment parameter values of a given simulation model represent regression or stochastic analysis derived values. (Col. 12, ll. 53-65). The reference further discloses that input variables utilized for fitting include in vitro and in vivo data. (Id.). In sum, the disclosure is limited to the fitting of data points so as to allow correlation different data sets, and providing a fitted adjustment parameter to provide a constant in a model, so as to minimize deviation of correlation is minimized. (Col. 13, ll. 1-35).

Therefore, the reference does not disclose the claimed limitation of a simulator reconfiguring one or more sensors. As such, this rejection should be withdrawn.

IV. Rejection under 35 USC 103

Claims 3 and 8 (new claims 37 and 42) were rejected as being obvious over Grass and further in view of Quellette (Industrial Physics, pages 11-12, 1998). This rejection is respectfully traversed.

As discussed in Section III(2) above, Grass is deficient with respect to the claimed limitations of independent claims 36 and 40. Further, similar to Grass, Quellette does not teach or suggest the claimed limitation of a simulator reconfiguring one or more sensors. As such, Grass alone or in combination with Quellette does not render obvious claims 37 and 42. Therefore, this rejection should be withdrawn.

CONCLUSION

Applicants respectfully solicit the Examiner to expedite the prosecution of this patent application to issuance. Should the Examiner has any questions or believes it would beneficial as to any issues above, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

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By: 

Ray Akhavan
Registration No. 58,120

WILSON SONSINI GOODRICH & ROSATI
650 Page Mill Road
Palo Alto, CA 94304-1050
(202) 973-8832
Client No. 021971